Research Article

Histopathological Changes in Gastric Mucosal Biopsies in Chronic Gastritis and Correlation of Pathological Features with Helicobacter Pylori Infection

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Abstract

Introduction: Diseases related to gastric acid account for nearly one third of all health expenditure on gastrointestinal (GI) diseases. Evaluation of morphological features in chronic gastritis using updated Sydney system has not been systematically evaluated in India. So this study was done to interpret the histopathological changes in chronic gastritis using updated Sydney system and to correlate these pathological features with Helicobacter pylori (H. pylori) infection. Methods Gastric mucosal biopsies in a tertiary care centre in north India were evaluated using routine histopathological methods. Histopathological changes in patients with chronic gastritis were interpreted using updated Sydney system and correlated with H. pylori infection. **Results**: Chronic gastritis was seen in 89 cases. Histological grading of chronic gastritis was done by updated Sydney system. Chronic inflammation was present in 100% cases, neutrophilic activity in 39.33% cases, intestinal metaplasia in 7.87% cases, glandular atrophy in 12.36% cases and lymphoid follicles in 29.21% cases. H. pylori were identified in 50.56% cases of chronic gastritis. Association of H. pylori with pathological features in chronic gastritis was evaluated. The association of H. pylori with degree of chronic inflammation, neutrophilic activity and lymphoid aggregates was statistically significant. **Conclusions**: Histopathology should be performed in all cases of chronic gastritis. The updated Sydney classification provides an objective histological evaluation of chronic gastritis. The grade of chronic inflammation, neutrophilic activity and lymphoid follicles are significantly associated with H. pylori infection. So search for H. pylori should be initiated if neutrophils and lymphoid follicles are seen in the antral biopsies.

Key words: Helicobacter pylori, gastritis, dyspepsia, endoscopy

Introduction:

Disorders of the stomach are a frequent cause of clinical disease, with inflammatory and neoplastic lesions being particularly common. Diseases related to gastric acid account for nearly one third of all health care spending on gastrointestinal (GI) diseases. Symptomatology of gastric diseases range from dyspepsia to altered bowel movements and dysphagia to GI bleed. Patients presenting with dyspepsia are often subjected to upper GI endoscopy as the first line of investigation. Endoscopic screening may detect mucosal lesions at an early stage especially atrophy, intestinal metaplasia and dysplasia so as to prevent progress of lesions to invasive cancer [1]. Biopsy sampling of gastric mucosa at diagnostic endoscopy provides information that cannot be obtained by other means. The most common

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indication for gastric biopsy is the need to know whether or not the patient is infected with H. pylori, and whether the stomach is gastritic or not. Microscopic examination of gastric biopsy specimens, in addition to H. pylori status, provides information about the grade, extent, and topography of gastritis-related and atrophy-related lesions in the stomach. It has been firmly established and known that the endoscopic findings in H. pylori gastritis do not correlate with histological changes. Biopsy provides an excellent opportunity for the clinician and histopathologist to correlate the clinical data, endoscopic findings and pathological lesions**.** H. pylori infection has been established firmly with the development of peptic ulcer, chronic active gastritis, chronic persistent gastritis, atrophic gastritis and gastric neoplasia including gastric adenocarcinoma and gastric mucosa associated lymphoid tissue lymphomas [2]. The reported prevalence of H. pylori in patients with functional dyspepsia ranges from 39-87% [3]. It is widely accepted that colonization of the gastric surface epithelium by H. pylori is commonly associated with type B chronic gastritis. H. pylori were seen in 77% cases of gastritis [4] and 80% cases of gastric ulcer [5]. The recognition that H. pylori play a pivotal role in the pathogenesis of several gastroduodenal pathologies makes its diagnosis necessary in many different circumstances and therefore investigation for this organism has become an integral part of upper GI endoscopy. To remove confusion in the diagnosis of various forms of gastritis, the Sydney system was introduced to produce a standardized approach to the histological interpretation of gastric biopsies [6]. The Sydney system was later on updated in Houston in 1994 [7] and the histological division of this classification utilized graded variables for evaluation of chronic gastritis. Government Medical College, Jammu is a tertiary care teaching hospital where facilities for diagnosis and treatment of GI diseases exist. The rate of chronic gastritis and H. pylori infection in India is high. Evaluation of morphological features in chronic gastritis using updated Sydney system and its correlation with H. pylori infection has not been systematically evaluated in India. Hence this prospective study was done to interpret the histopathological changes in chronic gastritis using updated Sydney system and to correlate these pathological features with H. pylori infection.

Materials and Methods:

This prospective study was conducted in the Department of Pathology, Government Medical College, Jammu over a period of one year (1st November 2012 to 31st October 2013). All biopsies obtained for various symptoms of dyspepsia like abdominal pain, bloating, heartburn, nausea, vomiting and postprandial fullness were included in the study. Exclusion criteria included absolute/relative contraindication to upper GI endoscopy and attempt at H. pylori eradication or acid suppressive therapy in the last 2 weeks. All patients had given informed consent for the study and a local ethics committee had approved the protocol. After overnight fasting, upper GI endoscopy was performed on selected patients using Fujinon EG-265WR fiber-optic gastroscope under local anaesthesia with 10% xylocaine spray. Gastric mucosal biopsies from body and antrum were taken in each case. The biopsies were then processed, cut into sections of 4 micrometer thickness, stained with Haematoxylin and Eosin (H&E) and modified Giemsa techniques. The slides were evaluated by two pathologists and morphological variables of chronic gastritis were graded as mild, moderate and severe according to updated Sydney system. The association between histological findings and H. pylori infection was assessed by means of chi square test. A probability value of less than 0.05 was considered statistically significant.

Results:

A total of 100 patients who presented with symptoms of dyspepsia were included in the study. Upper GI endoscopy was performed in all patients and endoscopic mucosal biopsies were taken for histopathological evaluation. All the biopsies with evidence of chronic gastritis were evaluated. The biopsies were analysed taking into consideration the various histological parameters such as chronic inflammatory infiltrate, inflammatory activity, glandular atrophy, intestinal metaplasia, H. pylori and presence of lymphoid follicles. Out of 100 patients, chronic gastritis was seen in 89% cases (89/100). Majority of cases were seen in the 31-40 years age group followed by 41-50 years age group (Table 1). There were 56 males and 33 female patients with an M: F ratio of 1.7: 1. Histological grading of chronic gastritis was done by updated Sydney system [8] (Table 2). Chronic inflammation was present in 89 (100%) cases of chronic gastritis out of which, 44 (49.44%) had mild, 38 (42.70%) had moderate and 7 (7.87%) had severe chronic inflammation. Neutrophilic activity was seen in 35 (39.33%) cases of which 22 (24.72%) had mild, 9 (10.11%) had moderate and 4 (4.49%)

had severe neutrophilic activity. Intestinal metaplasia was seen in 7 (7.87%) cases with 5 cases (5.62%) having mild and 2 cases (2.25%) having moderate intestinal metaplasia. Glandular atrophy was seen in 11 (12.36%) cases out of which 7 (7.87%) were of mild grade and 4 (4.49%) were of moderate grade. Lymphoid follicles and lymphoid collections were seen in 26 (29.21%) cases of chronic gastritis. H. pylori were identified in 45 (50.56%) cases of chronic gastritis on gastric mucosal biopsies. Out of these 45 (50.56%) cases, 23 (25.84%) had mild, 18 (20.22%) had moderate and 4 (4.49%) had severe H. pylori colonization (Table 2). Association of H. pylori and degree of inflammation in chronic gastritis was evaluated (Table 3). 16 out of 44 (36.36%) cases of chronic gastritis with mild chronic inflammatory cell infiltrate were positive for H. pylori whereas 23 out of 38 (60.53%) and 6 out of 7 (85.71%) cases of chronic gastritis with moderate and severe chronic inflammation were positive for H. pylori respectively. The association of H. pylori and degree of chronic inflammation was statistically significant (p value < 0.05). Further, association of H. pylori with activity, lymphoid aggregates, intestinal metaplasia and atrophy in chronic gastritis was also evaluated (Table 4). 35 cases of chronic gastritis showed activity. 30 of these 35 cases (85.71%) were positive for H. pylori. The association was statistically significant (p value <0.05). 26 cases of chronic gastritis showed lymphoid aggregates. 20 of these 26 cases (76.92%) were positive for H. pylori and the association was statistically significant (p value <0.05). 7 cases of chronic gastritis showed intestinal metaplasia and 2 out of these 7 cases (28.57%) were positive for H. pylori. The association was not statistically significant (p value >0.05). 11 cases of chronic gastritis showed atrophy. 7 out of these 11 cases (63.64%) were positive for H. pylori and the association was not statistically significant (p value >0.05).

Table 1: Age distribution in chronic gastritis

Age groups (years)	No. of cases	Percentage %
11-20	4	4.49
21-30	11	12.36
31-40	31	34.83
41-50	25	28.09
51-60	14	15.73
61-70	3	3.37
> 70	1	1.12

Table 2: Histological grading of chronic gastritis by updated Sydney system

Histological variables	Total	%	Grade	No.	%
Chronic Inflammation	89	100	Mild	44	49.44
			Moderate	38	42.70
			Severe	7	7.87
Activity	35	39.33	Mild	22	24.72
			Moderate	9	10.11
			Severe	4	4.49
Intestinal Metaplasia	7	7.87	Mild	5	5.62
			Moderate	2	2.25
			Severe	0	0
Atrophy	11	12.36	Mild	7	7.87
			Moderate	4	4.49
			Severe	0	0
H. pylori	45	50.56	Mild	23	25.84
			Moderate	18	20.22
			Severe	4	4.49

Table 3: Association of H. Pylori and degree of chronic inflammation in chronic gastritis

Inflammation	No. of Cases	H. pylori positive	Percentage %
Mild	44	16	36.36
Moderate	38	23	60.53
Severe	7	6	85.71

p Value <0.05

Table 4: Association of H. Pylori with activity, lymphoid aggregates, intestinal metaplasia and atrophy in chronic gastritis

Histological variables	Total cases	H. pylori positive	%	p Value
Activity	35	30	85.71	<0.0001
Lymphoid aggregates	26	20	76.92	0.003
Intestinal metaplasia	7	2	28.57	0.527
Atrophy	11	7	63.64	0.543

Discussion:

Chronic gastritis is a very common condition worldwide. The basic histological alteration is an increase in the chronic inflammatory cells in gastric mucosa. Chronic infection with H. pylori is now believed to account for the majority of cases of chronic gastritis [8].

There are two main mechanisms by which H. pylori may produce inflammation. Firstly, the organism may interact with surface epithelial cells producing either direct cell damage or the liberation of epithelium derived pro-inflammatory mediators. Secondly, H. pylori derived products may gain access to the underlying mucosa, thereby directly stimulating host non-specific and specific immune responses involving the liberation of variety of cytokine messengers [9].

Histopathological evaluation is the gold standard for diagnosis of this organism. In an attempt to remove confusion in the diagnosis of various forms of gastritis, the Sydney system was introduced in 1990 [6]. The Sydney system of grading and classification of gastritis was developed with the aim of producing a standardized approach to the histological interpretation of gastric biopsies. Its importance lies in the potential to maintain a common language among pathologists and to provide clinicopathological correlation [10].

The Sydney system was updated in Houston, Texas in 1994. The histological division of this classification utilizes graded variables which include chronic inflammation, neutrophilic activity, glandular atrophy, intestinal metaplasia and H. pylori density [7].

In the present study, maximum cases of chronic gastritis were seen in 31-40 and 41-50 years age group. A higher incidence was seen in males with an M: F ratio of 1.7: 1. Chen XY et al. [11] also found an M: F ratio of 1.8: 1.Histological grading of chronic gastritis was done by updated Sydney system. Chronic inflammation was present in 100% cases of chronic gastritis, out of which, 49.44% had mild, 42.70% had moderate and 7.87% had severe chronic inflammation similar to the results of Manxhuka-Kerliu S et al. [12].

Neutrophilic infiltration was seen in 39.33% cases with 24.72% patients having mild, 10.11% moderate and 4.49% severe neutrophilic activity. Garg B et al. [8] also observed neutrophilic activity in 33.33% cases of chronic gastritis.

Intestinal metaplasia was seen in 7.87% cases which is similar to the studies by Garg B et al. [8] and Atisook K et al. [13] who reported intestinal metaplasia in 7% and 8.2% cases respectively. Glandular atrophy was seen in 12.36% cases, out of which 7.87% had mild grade and 4.49% had moderate grade of atrophy. Garg B et al. [8], Atisook K et al. [13] and Dhakhwa R et al. [14] reported glandular atrophy in 12.33 %, 11.6% and 10% cases respectively. Lymphoid follicles and lymphoid collections were seen in 29.21% cases of chronic gastritis in the present study.

Figures:

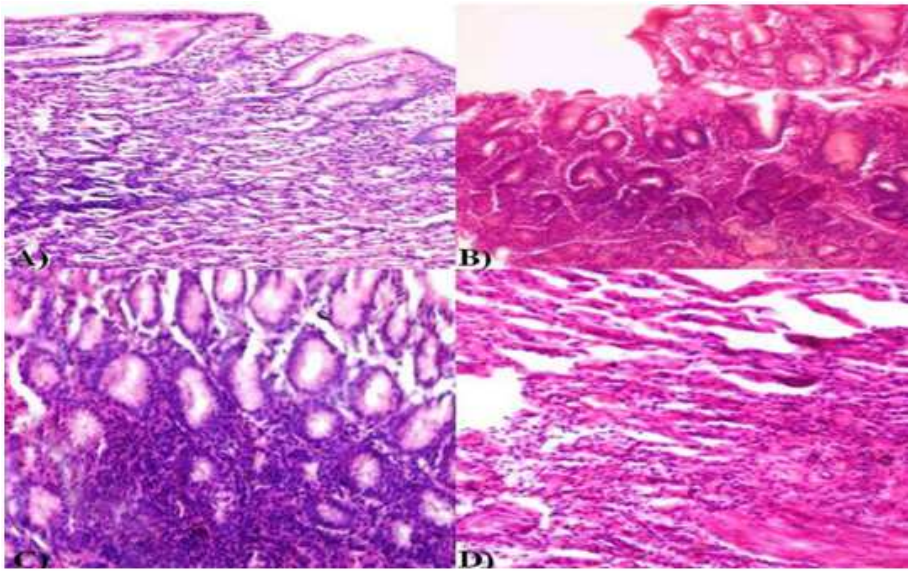

Figure 1: A) Photomicrograph (H&E, 10x) showing mild chronic body gastritis. B) and C) Photomicrographs (H&E, 10x) showing moderate and severe chronic antral gastritis respectively. D) Photomicrograph (H&E, 10x) showing moderately active chronic body gastritis.

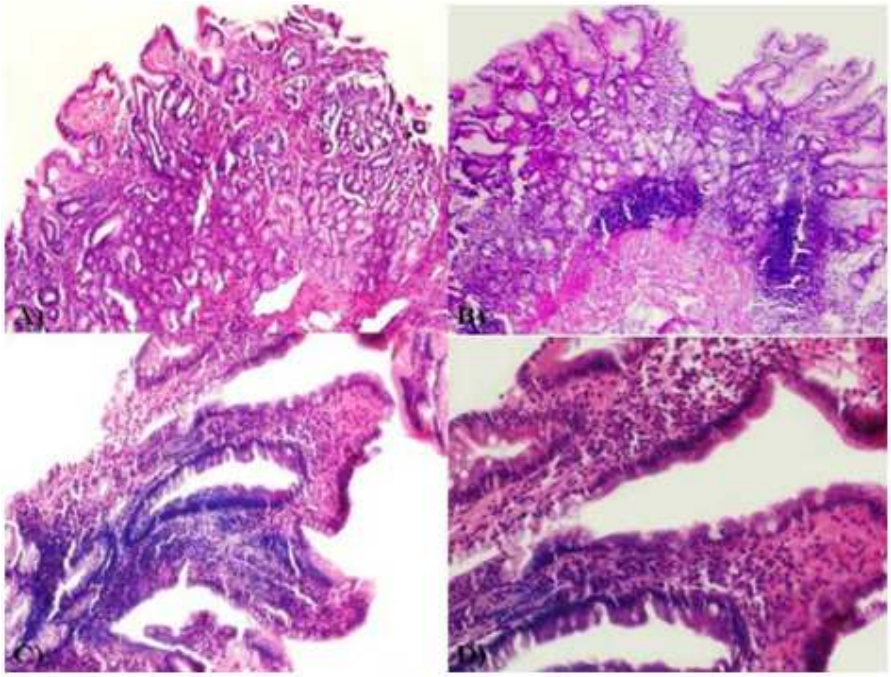

Figure 2: A) and B) Photomicrographs (H&E, 10x**)** showing chronic antral gastritis with mild glandular atrophy and presence of lymphoid follicles respectively. C) and D) Photomicrographs C) H&E, 10x and D) H&E, 20x showing moderately active chronic antral gastritis with foci of intestinal metaplasia and presence of goblet cells.

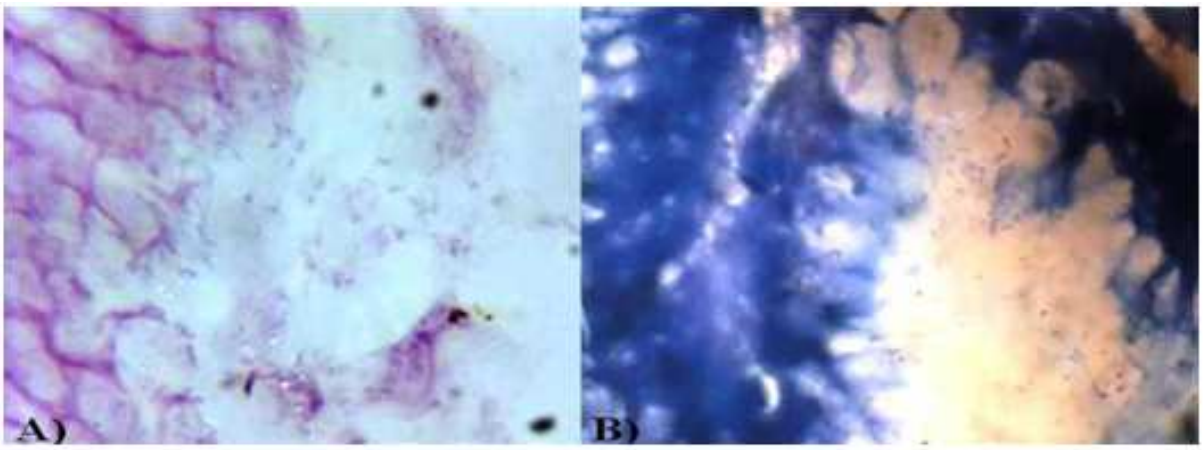

Figure 3: Photomicrographs A) H&E, 100x and B) Modified Giemsa, 100x showing numerous H. pylori on the surface of gastric mucosa.

50.56% cases of chronic gastritis were positive for H. pylori in the present study. The results were similar to previously published studies [15-16]. Association of H. pylori with degree of chronic inflammation, neutrophilic activity, lymphoid aggregates, intestinal metaplasia and atrophy in chronic gastritis was evaluated. 36.36% cases of chronic gastritis with mild inflammation and 60.53% cases of chronic gastritis with moderate inflammation were positive for H. pylori. H. pylori were positive in 85.71% cases of chronic gastritis with severe inflammation similar to Misra V et al. [17].

A significant association was seen between degree of chronic inflammation and H. pylori infection ($p<0.05$). Neutrophilic activity is an almost universal phenomenon in H. pylori gastritis. Biopsy specimens contain neutrophils in virtually all cases of H. pylori positive gastritis. Neutrophils are a very sensitive indicator for the presence or absence of H. pylori and disappear within days of cure of infection [18].

In the present study, 35 cases of chronic gastritis showed activity. 85.71% of these cases were positive for H. pylori and the association was statistically significant. Kalebi A et al. [19] in their study on superficial gastritis showed H. pylori infection in 91% of cases with neutrophilic infiltration.

Shafii M et al. [20] in their study concluded that activity had statistically significant association with H. pylori. 26 cases of chronic gastritis showed lymphoid aggregates. 76.92% of these cases were positive for H. pylori and the association was statistically significant ($p<0.05$). Genta RM et al. [21] found 91.8% prevalence of lymphoid follicles in patients with H. pylori infection. Chen XY et al. [11] concluded that lymphoid follicles and aggregates were found in the gastric antral mucosa of 76.0% patients with various H. pylori associated gastric diseases. 7 cases of chronic gastritis showed intestinal metaplasia.

Only 28.57% of these cases were positive for H. pylori and the association was statistically insignificant ($p>0.05$). Mysorekar VV et al. [22] observed significant association between H. pylori colonization and intestinal metaplasia in acid peptic disease patients. In the latter study, apart from Giemsa staining, Rapid Urease Test was done for H. pylori detection. The discrepancy in the present study may be due to inadequate sampling.

Also study by Craanen ME et al. [23] has shown that yield for H. pylori infection is reduced when intestinal metaplasia is present. 11 cases of chronic gastritis showed atrophy. 63.64% of these cases were positive for H. pylori. However, the association in the present study was not statistically significant ($p>0.05$).

Thus we conclude that histopathology should be performed in all cases of chronic gastritis. The updated Sydney classification provides an objective histological evaluation of chronic gastritis.

Also the grade of chronic inflammation, neutrophilic activity and lymphoid follicles are significantly associated with H. pylori infection. So search for H. pylori should be initiated if neutrophils and lymphoid follicles are seen in the antral biopsies.

The detection of H. pylori can help us plan treatment strategies to reduce the menace of this organism.

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